99. The receptor of Claim 84 wherein the receptor has at least a two-fold increased functional response for pyrimidine nucleotides over purine nucleotides.

100. The receptor of Claim 99 wherein in the presence of pyrimidine nucleotides, the receptor presents a functional response to lower concentrations of pyrimidine nucleotides than to purine nucleotides as well as an increased response to similar concentrations of pyrimidine nucleotides than to purine nucleotides.

REMARKS

Claims 70, 74, 80, and 84 have been amended to more clearly recite the claimed invention. Claims 93-100 have been added. Support for Claims 93-100 can be found in the original Claims. No new matter has been added herewith.

The changes made to the claims by the current amendment, including **[deletions]** and additions, are shown on an attached sheet entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this Amendment.

Rejection under 35 U.S.C. §112, first paragraph

Claims 70-79, 84, and 89 were rejected under 35 U.S.C. §112, first paragraph on the assertion that the specification was not enabling for an isolated receptor variant having at least 60% amino acid sequence homology with SEQ ID NO:1 (or nucleotide sequence SEQ ID NO:2).

However, The specification is enabling for the claims as amended for the following reasons. As indicated in the accompanying Declaration of Dr. Marc Parmentier and Exhibits A-C, subsequent to the priority date of the present application, Applicants and others have cloned receptors having at least 60% homology with SEQ ID NO: 2 using standard techniques familiar to those skilled in the art. In particular as shown in Exhibit A, a gene encoding a mouse receptor having 82% amino acid identity with the human sequence provided in SEQ ID NO: 2 was isolated using a probe derived from the human sequence. In addition, as shown in Exhibits B and C, subsequent to the priority date of the present application, a gene encoding a rat receptor having 84% or 83% amino acid identity to the human sequence was isolated. Thus, the present application does in fact enable those skilled in the art to isolate receptors having more than 60% homology with the amino acid sequence of SEQ ID NO: 2.

Furthermore, one of skill in the art can readily identify receptors having more than 60% homology to SEQ ID NO:2 by conducting a bioinformatic comparison of a query sequence to the sequence of SEQ ID NO: 2. A variety of software programs for determining homology levels are available to those skilled in the art, including the multiple sequence alignment program Pileup of the GCG package described on page 20, lines 19-26 of the specification. In addition, such software may be used to identify conserved regions which provide nucleotide binding activity.

Thus, with the sequence information and activation assays described in the specification, one of skill in the art would be able to obtain a receptor which has more than 60% homology to SEQ ID NO: 2 and binds nucleotides. For the foregoing reasons, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

New Claims

As required by *Ex parte Wirt*, 1905 C.D. 247,117 O.G. 599, Applicant has canceled non-elected Claims 81-83, 85-88 and 90. Thus, the number of pending claims is equal to that at the time the Final Office Action was mailed. Furthermore, since the added claims are all dependent claims , no new search is required.

Conclusion

In view of the above arguments and amendments, Applicants respectfully submit that the application is in condition for allowance. However, should there be any questions, the Examiner is respectfully requested to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: June 5, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

70. **(Amended)** An isolated receptor **[having at least a two-fold preference for pyrimidine nucleotides over purine]** which binds nucleotides, wherein said receptor has an amino acid sequence having more than 60% homology with the amino acid sequence shown in SEQ ID NO:2**[, wherein in the presence of pyrimidine nucleotides, the receptor presents a functional response to lower concentrations of pyrimidine nucleotides than to purine nucleotides as well as an increased response to similar concentrations of pyrimidine nucleotides than to purine nucleotides]**.

74. **(Twice Amended)** An isolated nucleic acid molecule encoding a receptor which **[has at least a two-fold preference for pyrimidine nucleotides over purine]**binds nucleotides, wherein said receptor has an amino acid sequence having more than 60% homology with the DNA sequence shown in SEQ ID NO:1**[, wherein in the presence of pyrimidine nucleotides, the receptor presents a functional response to lower concentrations of pyrimidine nucleotides than to purine nucleotides or an increased functional response to similar concentrations of pyrimidine nucleotides than to purine nucleotides]**.

80. **(Twice Amended)** An antisense probe having a sequence fully complementary to an isolated nucleic acid molecule encoding a receptor which **[has at least a two-fold preference for pyrimidine nucleotides over purine]**binds nucleotides, wherein said receptor has an amino acid sequence having more than 60% homology with the DNA sequence shown in SEQ ID NO:1**[, wherein in the presence of pyrimidine nucleotides, the receptor presents a functional response to lower concentrations of pyrimidine nucleotides than to purine nucleotides or an increased functional response to similar concentrations of pyrimidine nucleotides than to purine nucleotides]**.

84. **(Twice Amended)** A method for determining whether a ligand can activate a receptor **[having at least a two-fold preference for pyrimidine nucleotides over purine]**which binds nucleotides, wherein said receptor has an amino acid sequence having more than 60% homology with the amino acid sequence shown in SEQ ID NO:2, comprising the steps of:

preparing an extract from cells expressing the receptor;

isolating a membrane fraction from said extract;

contacting said membrane fraction with said ligand; and

assaying said membrane fraction for increased receptor activity, wherein increased activity indicates that said ligand is an activator of said receptor**[, wherein in the presence of pyrimidine nucleotides, the receptor presents a functional response to lower concentrations of pyrimidine nucleotides than to purine nucleotides or an increased functional response to similar concentrations of pyrimidine nucleotides than to purine nucleotides]**.

Please add the following claims:

93. The receptor of Claim 70 wherein the receptor has at least a two-fold increased functional response for pyrimidine nucleotides over purine nucleotides.

94. The receptor of Claim 93 wherein in the presence of pyrimidine nucleotides, the receptor presents a functional response to lower concentrations of pyrimidine nucleotides than to purine nucleotides as well as an increased response to similar concentrations of pyrimidine nucleotides than to purine nucleotides.

95. The isolated nucleic acid molecule of Claim 74 wherein the receptor has at least a two-fold increased functional response for pyrimidine nucleotides over purine nucleotides.

96. The isolated nucleic acid molecule of Claim 95 wherein in the presence of pyrimidine nucleotides, the receptor presents a functional response to lower concentrations of pyrimidine nucleotides than to purine nucleotides as well as an increased response to similar concentrations of pyrimidine nucleotides than to purine nucleotides.

97. The antisense probe of Claim 80 wherein the receptor has at least a two-fold increased functional response for pyrimidine nucleotides over purine nucleotides.

98. The antisense probe of Claim 97 wherein in the presence of pyrimidine nucleotides, the receptor presents a functional response to lower concentrations of pyrimidine nucleotides than to purine nucleotides as well as an increased response to similar concentrations of pyrimidine nucleotides than to purine nucleotides.

99. The receptor of Claim 84 wherein the receptor has at least a two-fold increased functional response for pyrimidine nucleotides over purine nucleotides.

100. The receptor of Claim 99 wherein in the presence of pyrimidine nucleotides, the receptor presents a functional response to lower concentrations of pyrimidine nucleotides than to purine nucleotides as well as an increased response to similar concentrations of pyrimidine nucleotides than to purine nucleotides.